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Clinical hypertension research in patients with atrial fibrillation: At last!

Anastasios Kollias MD, PhD 🅾 | **Konstantinos G. Kyriakoulis MD** 🅾 |
George Stergiou MD, PhD, FRCP 🅾

Hypertension Center STRIDE-7, National and Kapodistrian University of Athens, School of Medicine, Third Department of Medicine, Sotiria Hospital, Athens, Greece

Correspondence: Anastasios Kollias, MD, PhD, Hypertension Center STRIDE-7, National and Kapodistrian University of Athens, School of Medicine, Third Department of Medicine, Sotiria Hospital,152 Mesogion Avenue, Athens 11527, Greece.
Email: taskollias@gmail.com

The prevalence of atrial fibrillation (AF) and hypertension increases with age and their coexistence significantly increases the risk of stroke, especially in elderly. Blood pressure (BP) measurement in patients with AF is difficult and uncertain due to inherent increased beat-to-beat BP variability, and AF patients represent a classic exclusion criterion in hypertension clinical trials leading to limited research data. In this issue of the *Journal of Clinical Hypertension*, Kario et al[1] assessed BP control in elderly patients with non-valvular AF based on office (OBP) and home (HBP) BP measurements. The authors showed that among 4936 AF patients with hypertension, mainly treated, 28%, 13%, 23%, and 36% had well-controlled, white-coat, masked and sustained hypertension, respectively.[1] This is the first study to report hypertension phenotypes in a large sample of AF patients with hypertension using OBP and HBP. These findings are in line with respective studies in non-AF patients, and stress the role of out-of-office BP monitoring for the accurate assessment of BP control also in AF hypertensives since OBP measurements are often misleading.[2] However, this study raises important additional research questions including: (a) how accurate is BP measurement in AF and which method should be used? (b) do classic office BP measurements in AF have prognostic ability? (c) what is the role of out-of-office BP monitoring in AF? (d) are the established BP thresholds and targets applicable in AF patients?

The accuracy of BP measurement is crucial in AF patients as in sinus-rhythm individuals. The 2018 guidelines by the European Society of Cardiology/European Society of Hypertension (ESC/ESH) state that *"additional BP measurements may have to be performed in patients with unstable BP values due to arrhythmias, such as in patients with AF, in whom manual auscultatory methods should be used as most automated devices have not been validated for BP measurement*

in patients with AF."[3] However, this statement in favor of the auscultatory method comes in contrast with the clinical practice where automated oscillometric BP monitors are increasingly used for OBP measurement, and almost exclusively used for out-of-office BP monitoring (home and ambulatory [ABP]). In the study by Kario et al, validated mercury, aneroid, or electronic sphygmomanometers (as per the method routinely used at each institution) were used for OBP and upper-arm cuff automated oscillometric BP monitors for HBP monitoring.[1] The evidence from validation studies of automated electronic BP monitors in AF is limited and methodologically heterogeneous.[4] A recent meta-analysis suggested reasonable accuracy in measuring systolic BP (pooled average systolic BP difference 1.0 mmHg, 95% CI −0.1, 2.1), and a small yet consistent overestimation of diastolic BP (2.1 mm Hg, 95% CI 0.1, 4.0).[4]

The 2019 AAMI/ESH/ISO Universal Standard (ISO 81060-2:2018) for the validation of BP monitors refers to AF patients as a *"special population"* requiring separate validation, yet it is stated that *"there is no agreed reference BP measurement and validation procedure for patients with AF."*[5] Thus, a validation protocol specifically for AF patients needs to be developed. Recently, a modified validation procedure of the Universal Standard (ISO 81060-2:2018) was applied to validate a novel professional oscillometric upper-arm cuff device (Microlife WatchBP Office), which has an algorithm for detecting AF and then applies a BP measurement algorithm which is specific to AF.[6] The device algorithm fulfilled all the validation criteria in AF patients despite the expected high reference BP variability which made the validation test more difficult to pass.[6] Such advances in automated BP measurement technology are reassuring for employing professional automated BP measurement in AF patients.[6]

Another crucial research question is whether the usual BP measurements in clinical practice have prognostic ability in AF patients. Prospective outcome trials specifically designed for this purpose are lacking. A recent meta-analysis of studies evaluating oral anticoagulants in AF patients showed that usual OBP measurements and hypertension diagnosis predicted stroke or systemic embolism, whereas follow-up OBP control appeared to have even stronger predictive ability than baseline OBP.[7] It should be mentioned that there was considerable heterogeneity in the OBP methodology, which was not standardized in most studies (auscultatory or automated method, usually single readings).[7] Despite these methodological flaws, classic OBP measurements predicted outcome in AF patients.

The study by Kario et al[1] is unique in that HBP monitoring was employed to assess hypertension control in treated hypertensives with AF. To date, out-of-office BP monitoring (both HBP and ABP) has been discouraged in patients with AF due to the assumption that the automated devices are unable to measure BP or are inaccurate due to the presence of arrhythmia. However, accumulating evidence suggests that the frequency of errors and the measurement accuracy of the automated BP monitors in patients with hemodynamically stable AF is reasonable.[4] Thus, HBP and ABP monitoring should be routinely used in the evaluation of hypertension in AF patients, as in those with sinus rhythm.[4,8]

Another important issue is that strict systolic BP targets were used in the study by Kario et al for OBP (<130 mm Hg) and HBP (<125 mm Hg) control.[1] This should also take into account the old average age of the participants (>80 years). Indeed, the authors acknowledged that HBP monitoring might result in an overestimation of the BP level in some elderly patients, such as those with orthostatic hypotension, and more studies are needed to justify a strict HBP target in the very elderly population.[1] The elderly represent a highly heterogeneous group depending on their frailty status and ESC/ESH guidelines recommend a more conservative treatment strategy for frail and those older than 80 years.[3] Moreover, the relationship between BP measurement methods differs across the age range, with the elderly having higher HBP values than awake ambulatory BP.[9] In addition, the elderly appear to have more often masked hypertension on HBP but not ABP than the reverse, the latter being more common in younger hypertensives.[10] These findings along with the slight overestimation of systolic BP by the oscillometric method in AF and the fact that AF is more prevalent in the elderly should lead to a more conservative strategy in this population until further studies become available.

In conclusion, accumulating data suggest that in patients with stable AF, automated office BP measurement is reasonably accurate and has prognostic value. Moreover, out-of-office BP monitoring (HBP and ABP) using automated devices is feasible. Standardization of BP measurement methodology in and out of the office and proper validation of novel automated BP monitors in AF is necessary. AF patients should not be excluded anymore from clinical research trials in hypertension.

CONFLICT OF INTEREST
None.

ORCID
Anastasios Kollias https://orcid.org/0000-0002-2098-1665
Konstantinos G. Kyriakoulis https://orcid.org/0000-0001-8986-2704
George Stergiou https://orcid.org/0000-0002-6132-0038

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